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BARBRE

Ortho-Chloro-Benzoyl-Acetic Ester and some of its Derivatives

Chemistry

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ORTHO-CHLORO-BENZOYL-ACETIC ESTER AND SOME OF ITS DERIVATIVES

BY

CLARENCE BARBRE

THESIS

FOR THE

DEGREE OF BACHELOR OF SCIENCE

IN

CHEMISTRY

COLLEGE OF LIBERAL ARTS AND SCIENCES

UNIVERSITY OF ILLINOIS

1914

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May 30th 1914

This is to certify that the Thesis prepared
Clarence Barbre,

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equirement for the
ence.

Lambert Thorp.

approved:

Dr. Thorp was called out of town by the death of his father before he signed the certificate.

W. A. Noyes

Instructor in Charge

APPROVED: W. A. Noyes

HEAD OF DEPARTMENT OF Chemistry

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May 30th 1914

This is to certify that the Thesis prepared under my supervision by Clarence Barbre, entitled:

Ortho-chloro Benzoylacetic acid and some of its Derivatives is approved by me as fulfilling this part of the requirements for the Degree of Bachelor of Science.

Lambert Thorp.

approved:

Instructor in Charge

APPROVED: W. A. Noyes

HEAD OF DEPARTMENT OF Chemistry

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UNIVERSITY OF ILLINOIS

May 25 1914

THIS IS TO CERTIFY THAT THE THESIS PREPARED UNDER MY SUPERVISION BY

Clarence Barbre

ENTITLED ORTHO-CHLORO-BENZOYL-ACETIC ESTER AND SOME OF ITS DERIVATIVES

IS APPROVED BY ME AS FULFILLING THIS PART OF THE REQUIREMENTS FOR THE

DEGREE OF Bachelor of Science

Instructor in Charge

APPROVED: W. A. Noyes

HEAD OF DEPARTMENT OF Chemistry

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INTRODUCTION.

Ever since the discovery of acetoacetic ester in 1863 by Geuther, who prepared the sodium salt while trying to replace with sodium the second hydrogen atom in ethylacetate by contact with metallic sodium, acetoacetic ester and its derivatives and homologues has been the subject of much study and research.

To Wislicenus, perhaps more than to any other, is due the credit for the knowledge of the numerous transformations which acetoacetic ester undergoes; the formation of the mono- and di- alkyl derivatives and the conditions which determine the ketonic and acid hydrolysis and the synthetic method for the preparation of acids and ketones by a combination of the two processes is due to him.

To Claisen we are indebted for the best explanation of the mechanism of the reaction, for it was he who proved that the active condensation agent was not metallic sodium, as was first believed, but that the reaction was started by the formation of sodium ethylate due to a trace of alcohol in the sodiumacetate. He also showed that the reaction, as first carried out, was the result of two reactions; an intermediate addition product being formed, and that this again reacting with another molecule of sodium ethylate produces the ester. "This view", says Cohen in his "Organic

Chemistry", "explained the enolic structure of the sodium compound, which was by this time generally recognized." The most convincing proof of the active agency of sodium ethylate has been the large number of syntheses that have been made by means of this agent.

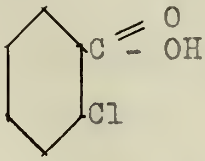
ORIGIN AND NATURE OF THE WORK.

In order to continue the work of preparing and studying some of the derivatives of benzoylacetic ester, which was begun by William J. Hale and Lambert Thorp, the preparation of ortho-chloro-benzoylacetic ester and some of its derivatives was attempted.

For the preparation of this ester anthranilic acid was diazotised and chlorine substituted for the amino group, thus forming ortho-chlorobenzoic acid; this in turn was converted to the acid chloride by treating with phosphorus pentachloride. This was taken through the acetoacetic ester synthesis to obtain the sodium salt of ortho-chloroacetoacetic ester, which was then transformed to ortho-chlorobenzoylacetic ester by the action of dilute ammonia. The ester was taken through a ketonic decomposition by boiling with dilute sulphuric acid whereupon ortho-chloroacetophenone was produced. The structure of the mono-nitro product of this ketone was determined by the oxidation to the acid, which had already

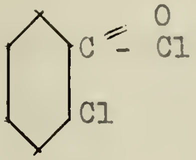
been prepared and characterized. The oxime of ortho-chloroacetophenone and ortho-chlorobenzoyl acetic acid were also prepared.

ORTHO-CHLOROBENZOIC ACID.



Twenty grams of crystallized cupric chloride, 10 gms. of powdered copper, 80 cc. of concentrated hydrochloric acid and 20 cc. of water were heated in a flask until colorless. While the solution was cooling 50 gms. of anthranilic acid were diazotised. The acid was dissolved in 250 cc. of water and 100 cc. of concentrated hydrochloric acid. Ice was added and a solution of 27 gms. of sodium nitrite in 200 cc. of water was poured in gradually. The cooled cuprous chloride solution with a few pieces of ice was placed in a two litre beaker into which the diazonium solution was poured in a thin stream. Nitrogen was evolved and a white curdy precipitate, underlying a bluish-green solution, resulted. The whole was allowed to stand over night, after which the product was separated by means of a Büchner funnel. The acid was recrystallized from hot water. It was pure white and melted at 229°C. The yield was 84.5% of the theoretical amount.

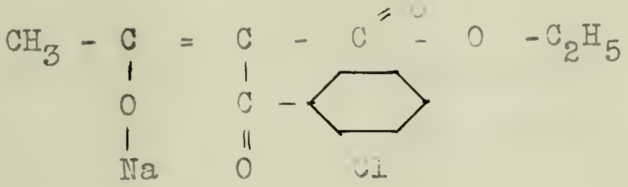
ORTHO-CHLOROBENZOYL CHLORIDE.



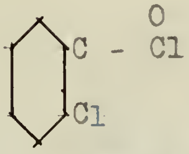
To 50 gms. of ortho-chlorobenzoic acid in a 500 cc. round-bottomed flask, 68 gms. of phosphorus pentachloride were added in portions. The dry mixture reacted in the cold with evolution of hydrochloric acid. After the first vigorous reaction had ceased heat was applied and the reaction driven to completion. The dark liquid which resulted was transferred to a 150 cc. distilling bulb connected to a water condenser and heated until the phosphorus exychloride had distilled. At the temperature of 150°C. all of the phosphorus had been removed and the water condenser was exchanged for an air condenser. The temperature rose rapidly and the fraction coming over between 225°C. and 230°C. was collected and redistilled. The acid chloride was obtained as a colorless oil, which, upon standing, turned yellow as do benzoyl chloride and benzoyl bromide. Yield 74.8% of theory.

SODIUM SALT OF ORTHO-CHLOROBENZOYLACETOACETIC ESTER.

Three hundred and twenty cc. of absolute alcohol were placed in a 500 cc. round-bottomed flask, fitted with a reflux condenser, and 20.8 gms. of clean sodium were added in portions. The reaction slowed up towards the end of the addition and heat was applied. After all reaction had ceased the contents of the flask were cooled to about 15°C. and measured.



1. $2\ C_2H_5OH + 2\ Na \longrightarrow 2\ C_2H_5O\ Na + H_2$
2. $CH_3 - COCH_2CO_2C_2H_5 + NaOC_2H_5 \longrightarrow 1\ CH_3.\ C(ONa):\ CH.CO_2C_2H_5$ $+ 1\ C_2H_5OH.$
3. $2\ CH_3.\ C(ONa):\ CH.CO_2C_5H$ +
   29.25 gms.



39.25 gms.

→ 1 acetoacetic ester + Na salt of ortho-chlorobenzoylaceto-acetic ester + NaCl.

4. 29.25 gms. acetoacetic ester + NaO Et. give reactions (2) and (3).

On account of the fact that the whole scheme of Claisen's synthesis is based on the control of the concentration

of the reacting molecules the volume had to be made up to 320 cc. For this 21 cc. were necessary. The preparation of the sodium salt was carried out in the manner described by Claisen for the preparation of benzoylacetoacetic ester, the benzoyl chloride being replaced by ortho-chlorobenzoyl chloride. According to this method, as shown by the preceeding reactions, one-half of the sodium acetoacetic ester present is transformed into acetoacetic ester, consequently further additions of sodium ethylate are made to reform the sodium salt, and this in turn is allowed to act with the acid chloride which is added immediately after the proper temperature is reached. The reaction may be indicated as follows:

2 Na acetoacetic ester + orthochlorobenzoyl chloride
NaCl + acetoacetic ester + Na salt of ortho-chlorobenzoylacetoacetic ester.

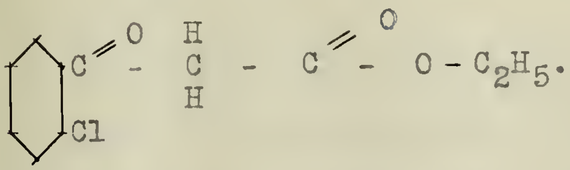
Procedure:

The entire quantity of acetoacetic ester (58.5 gms.) was mixed with 160 cc. of the sodium ethylate solution, cooled to 5°C., in a 600 cc. beaker. Into this solution were then added from a burette, 31.20 cc. (39.25 gms.) of the acid chloride. The mixture was constantly stirred and the temperature kept below 10°C. A white pasty mass formed. After standing thirty minutes the second portion, (one half of that remaining) 80 cc. of the sodium ethylate solution

was added, the mixture brought to 5°C. and the corresponding portion, 15.6 cc. of the acid chloride added as before. After a lapse of another period of thirty minutes the third portion of these solutions, 40 cc. of sodium ethylate and 7.8 cc. of the acid chloride, were similarly added. In like manner were added the fourth and fifth portions, each consisting of 20 cc. sodium ethylate and 3.9 cc. of the acid chloride, thus completing the additions.

The entire reaction mixture was now allowed to stand in the ice box for ten hours, when the separation of the sodium salt was complete. It was filtered by suction and washed with dry ether. Yield 122.3 gms.

ORTHO-CHLOROBENZOYLACETIC (ETHYL) ESTER.

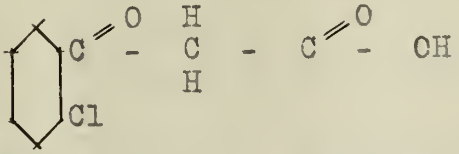


One hundred and twenty gms. of the sodium salt prepared above, were dissolved in 600 cc. of water, 54 gms. of ammonium chloride and 60 cc. of ammonium hydroxide were added, and the mixture kept at 40° - 50°C. for three hours with frequent shaking. The ester which separated as a heavy oil was extracted three times with 75 cc. portions of ether. The ethereal solution was dried over calcium chloride and the ether distilled. After being dried in a vacuum desiccator

over sulphuric acid the ester weighed 55 gms. Attempts to distil the ester under 30 mm. pressure resulted in its decomposition. Ortho-chlorobenzoylaceticethyl ester in a pale yellow, oily liquid, heavier than water in which it is insoluble. Its odor is faint and not unpleasant. Determinations on the per cent. of chlorine by the Stephanow-Volhard method gave the following results:

Calculated for	Found
$C_{11}H_{11}O_3Cl$	14.4
	14.9
15.64	15.1

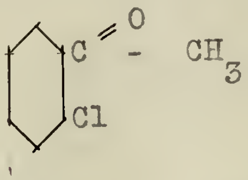
ORTHO-CHLOROBENZOYLACETIC ACID.



This acid was prepared by allowing 5 gms. of the ester to stand at room temperature with a 5% excess of a 3% potassium hydroxide solution for a period of forty-eight hours. When first mixed by shaking, some solid particles separated out. On standing, it appeared that a large part of the solid had gone into solution. There was a faint odor of the ester present and also of acetophenone. The mixture was extracted and attempts made to obtain the acid in a pure state but press of other work prevented the isolation of the acid.

KETONIC DECOMPOSITION OF ORTHO-CHLOROBENZOYLACETIC ESTER

ORTHO-CHLOROACETOPHENONE



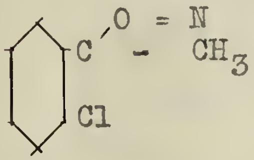
In a 500 cc. flask, fitted with a reflux condenser, 53.5 gms. of the ester, 60 cc. of concentrated sulphuric acid, and 240 cc. of water were boiled for about fourteen hours. At the end of this time all of the carbon dioxide seemed to have been evolved and no trace of the odor of the ester remained. However, the mixture was extracted with ether and the ethereal solution was washed with a 10% solution of potassium hydroxide to remove any possible trace of the ester. The ethereal solution was dried over calcium chloride, filtered and distilled. The portion coming over between 223°C. and 226°C. was collected and redistilled. Yield 80% of theory. Determinations on the per cent. of chlorine gave the following results:

Calculated for	Found
$C_8H_7O\ Cl$	24.25%
22.94%	22.38
	22.90

Ortho-chloroacetophenone is a colorless transparent oil, the odor of which resembles that of acetophenone. It is insoluble in water, but miscible in the common organic liquids.

The boiling point at 738 mm. is 227 - 228°C.

THE OXIME OF ORTHO-CHLORO ACETOPHENONE.



Three gms. of hydroxylamine hydrochloride were added to 2 gms. of sodium hydroxide in 10 cc. of water and 5 gms. of the ketone added. Alcohol was added to homogeneity, 20 cc. being required. The whole was corked up in a flask and allowed to stand for three hours when white needles had begun to form. The mixture was allowed to remain thus for an additional three days though twenty-four hours might have been sufficient judging from the increase in the quantity of crystals. The oxime was filtered off and washed with cold water. Upon the addition of hot water to the filtrate a further formation of crystals occurred. The oxime was recrystallized from a hot 50% solution of alcohol and water. The oxime of ortho-chloroacetophenone crystallizes in beautiful, snow-white needles which melt at 117°C. It is insoluble in water, is slightly soluble in absolute alcohol. Determinations on the per cent. of nitrogen by the combustion method gave the following results:

Calculated for	Found
$C_8H_7O\ Cl\ N$	8.56
Theory 8.26%	

NITRATION OF ORTHO-CHLOROACETOPHENONE.

About ten per cent. excess of nitric acid was used in the following manner: 50 cc. of concentrated sulphuric acid and 4 cc. of nitric acid (sp.gr. 1.48) were mixed and cooled to zero degrees. Ten grams of the ketone were added slowly from a dropping funnel while the mixture was stirred and the temperature maintained at 10°C. The resulting mixture was allowed to stand 10 to 12 hours when it separated into three portions; floating on top was a light yellow solid, below was the liquid layer of sulphuric acid, unreacted ketone, and dissolved products of the reaction. At the bottom there was usually a large drop of heavy red oil that contained for the most part unreacted ketone.

The reaction mixture was poured into cole water when a copious white precipitate formed. The solid, and red oil were filtered off from the acid and washed with cold water. The product was then washed with ether to remove the red oil, whereupon, as was later found, the acid which had been formed by a secondary oxidation was also extracted. The nitro-ketone is a pure white solid which melts sharply at 183°C. It is insoluble in water, very slightly soluble in alcohol or ether and more soluble in benzene from which it was recrystallized. Determinations on the percent. of chlorine gave the following results:

Calculated for $C_8H_7O_3N\ Cl$	Found
20.25%	20.00%
	19.90

DETERMINATION OF THE STRUCTURE OF NITRO-CHLOROACTEOPHENONE.

Two grams of chloronitroacetophenone with 4.7 grams of potassium permanganate in 235 cc. of water (approximately a 2% solution) were placed in a flask fitted with a reflux condenser, and boiled until the solution had become colorless. After the manganese dioxide had been separated by filtration the clear filtrate was evaporated almost to dryness and then acidified with concentrated hydrochloric acid. The precipitated acid, after recrystallization from hot water showed a melting point of 163.(uncorrected). This melting point compares favorably with that (165 C) for 2-chloro-5-nitro benzoic acid. Hence the nitro ketone must have the chlorine and nitro groups in the 2 and 5 positions respectively in reference to the acetyl group.

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